

Scale Loss Score (SLoS): a novel measure of drug benefit-risk assessment

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Introduction

- ▶ **MultiCriteria Decision Analysis (MCDA)** is a popular quantitative method to assess the **benefit-risk (BR) balance** of treatments: it permits to summarize the benefits and the risks of a drug in a **single utility score**
- ▶ The utility score is often derived using a **linear model** which might lead to **counter-intuitive conclusions**, for example, a recommendation of a non-effective drug
- ▶ We propose **Scale Loss Score (SLoS)** as a new tool for benefit-risk assessment: it is based on strong theoretical principles, addresses the issues of the linear MCDA model and can lead to more **meaningful recommendations**

Notations

ξ_{ij} : performance of treatment i on criterion j , $j = 1, \dots, n$

$u_j(\xi_{ij})$: linear partial value functions - map the performances on criterion j to a (0, 1) scale
 $u_j(\xi_{ij}) = \frac{\xi_{ij} - \xi'_{ij}}{\xi''_{ij} - \xi'_{ij}}$, ξ'_{ij} and ξ''_{ij} the worst and best values

w_j and \tilde{w}_j : weight reflecting the importance of criterion j

Linear MCDA

MCDA linear utility score:

$$u(\xi_i, \mathbf{w}) := \sum_{j=1}^n w_j u_j(\xi_{ij})$$

Higher utility score → more preferable BR balance

SLoS

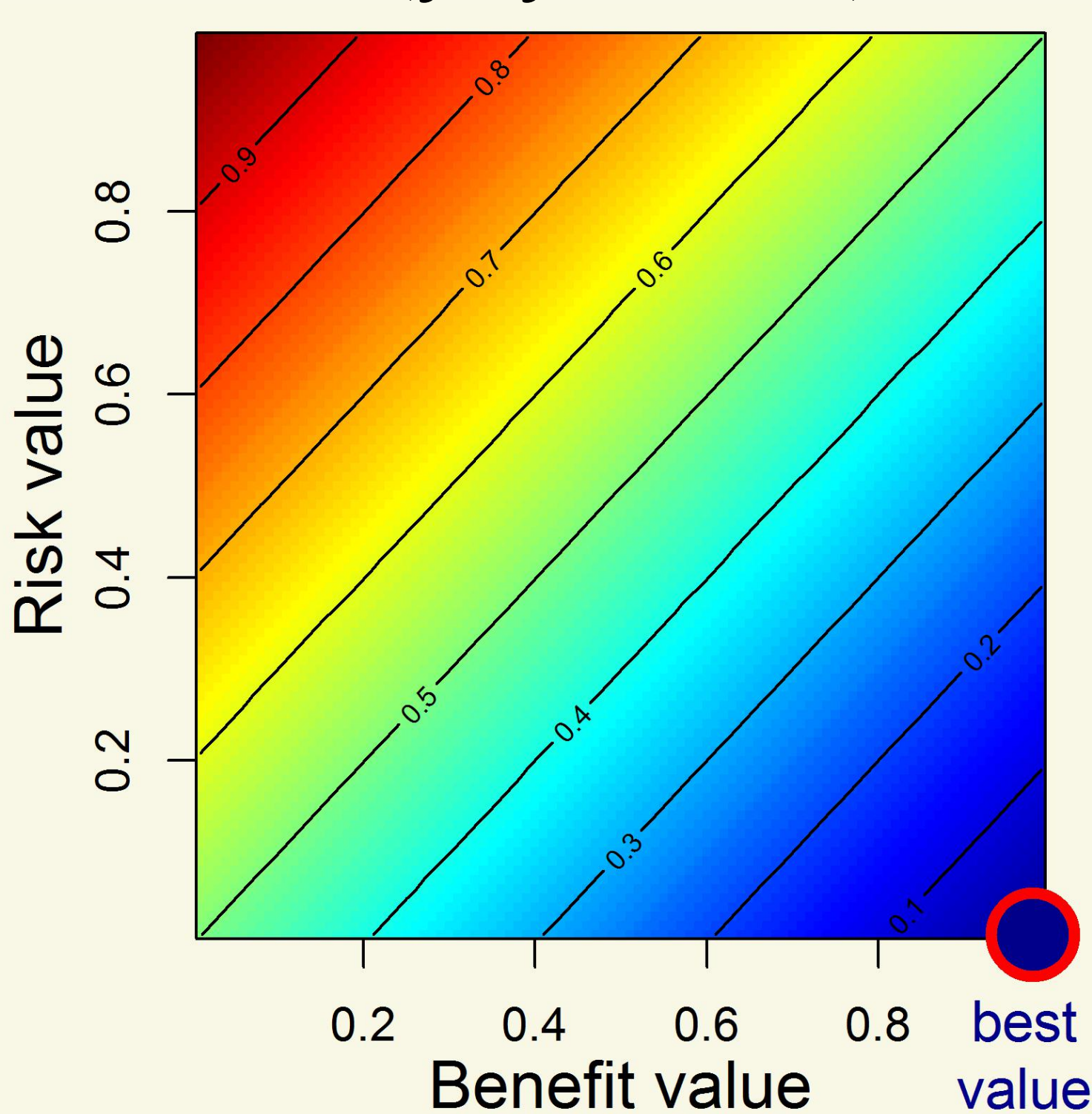
Scale Loss Score (SLoS):

$$l(\xi_i, \tilde{\mathbf{w}}) := \sum_{j=1}^n \left(\frac{1}{u_j(\xi_{ij})} \right)^{\tilde{w}_j}$$

Lower loss score → more preferable BR balance

Contours of

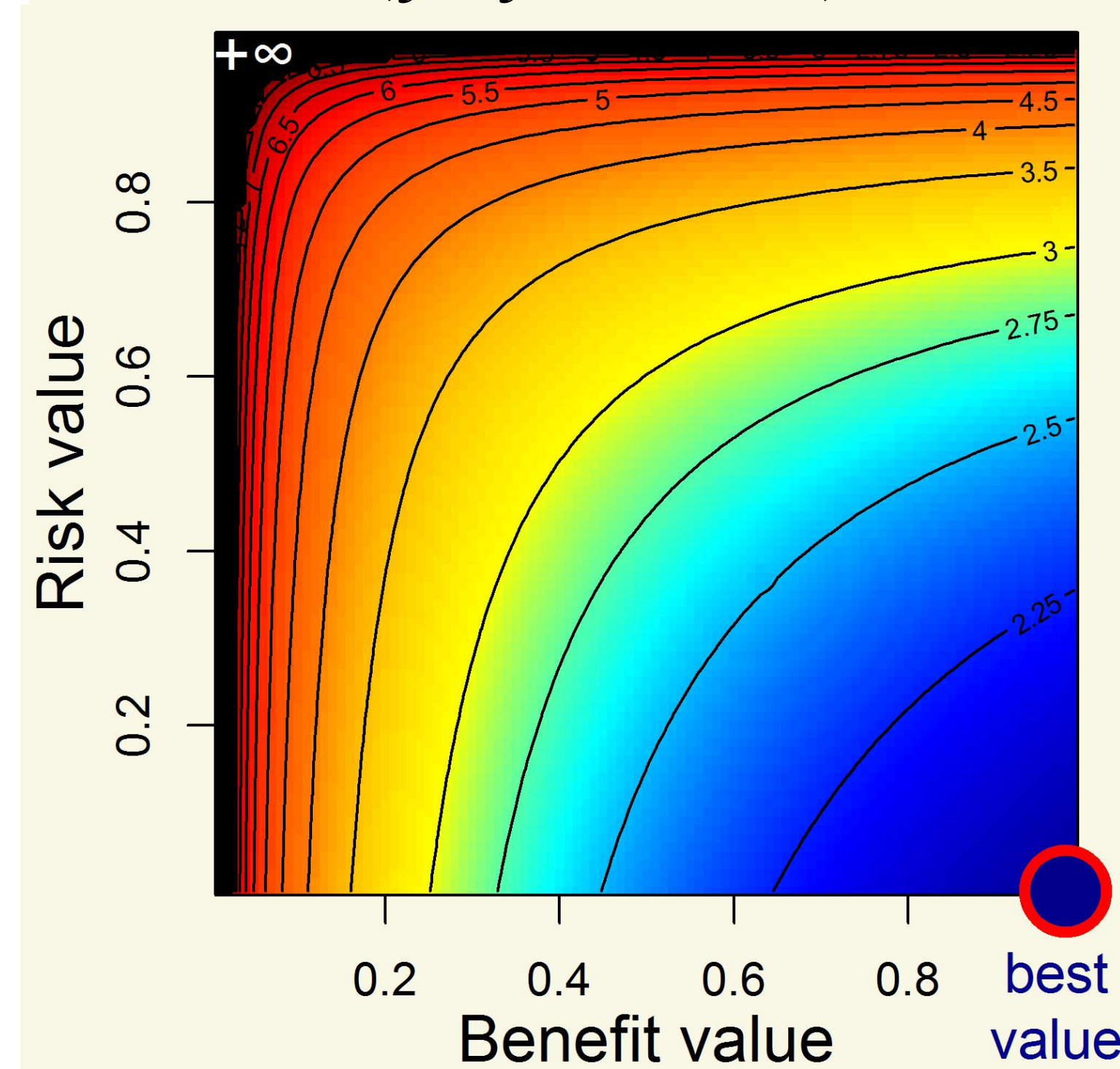
$$1 - u(\xi_{i1}, \xi_{i2}, w = 0.5)$$



- ▶ Benefit-risk trade-off is the **same** for all values of risk / benefit
- ▶ Drugs with no benefit or extreme risk **can be** recommended

Contours of

$$l(\xi_{i1}, \xi_{i2}, \tilde{w} = 0.5)$$



- ▶ For a given increase in benefit, a **smaller** increase in risk is tolerated if benefit is high than if it is low
- ▶ Drugs with no benefit or extreme risk **can never be** recommended

Examples

Fictive examples

2 criteria, fixed parameter values and $w = \tilde{w} = 0.25$

	Example 1		Example 2	
	Low benefit and risk	High benefit and risk	Drug 1	Drug 2
	Drug 1	Drug 2	Drug 1	Drug 2
Benefit	0%	30%	96%	50%
Risk	9%	20%	100%	85%
MCDA	0.6825	0.6750	0.2400	0.2375
SLoS	$+\infty$	2.5334	$+\infty$	5.3381

→ SLoS strongly penalizes extremely low benefit values and extremely high risk values

Case study: telithromycin

IMI PROTECT Benefit-Risk Group example

Proba(telithromycin > β-lactam antibiotics)

	Community Acquired Pneumonia (CAP)	Acute Bacterial Sinusitis (ABS)
MCDA	59%	71%
SLoS	51%	55%

→ SLoS results are more in line with the regulatory authorities concerns on ABS indication (CHMP reassessment and FDA removal)

Conclusion

Results of simulations comparing MCDA and SLoS:

- ▶ Both are robust to correlations between outcomes
- ▶ Similar conclusions in many cases
- ▶ Clear advantage of SLoS when drugs have no benefit or extreme risk

Scale Loss Score (SLoS) is a novel, simple and valuable tool for BR assessment

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